

Who's at Risk?

Gauging Susceptibility to Air Pollutants

What makes one individual more susceptible than another to the harmful effects of air pollution? If particulate matter (PM) differentially affects certain populations, which factors or characteristics are most likely to account for the heightened risk? These are the questions behind a new review of studies that examined various characteristics linked with susceptibility [*EHP* 119(4):446–454; Sacks et al.].

To assess the differential effects of PM on specific populations, epidemiologic studies often conduct stratified analyses; a stronger association between PM and the health effect being measured in one subgroup compared with another provides evidence for a more susceptible population. Additional insight can be gleaned via controlled

Biomonitoring studies have shown that children are especially vulnerable to the health effects of PM exposure.



Epigenetics of Formaldehyde

Altered microRNAs May Be Key to Adverse Effects

Formaldehyde has long been associated with asthma, acute respiratory illness, and nasopharyngeal cancer. The International Agency for Research on Cancer has deemed it a known human carcinogen. A new study reveals evidence that epigenetic mechanisms may contribute to links between formaldehyde exposure and respiratory illness [*EHP* 119(4):494–500; Rager et al.]. The study authors discovered that formaldehyde disrupts levels of microRNAs, or miRNAs, small regulatory molecules that play a key role in gene expression.

Ambient air contains formaldehyde given off from car exhaust, incinerators, and manufacturing and power plants. Formaldehyde also is widely used in preservatives and adhesives, including glue that binds plywood and particleboard, and it offgasses from furniture and building materials that use these products.

Despite formaldehyde's known respiratory toxicity, little is known about its mechanism of action related to disease. The

human exposure studies (which examine individuals with a preexisting disease) and toxicologic studies using animal models of disease. The authors of the current study integrated these various lines of evidence to determine whether there was coherence of associations across the scientific disciplines. They also assessed the biological plausibility of specific characteristics identified in epidemiologic studies as potentially conferring susceptibility to PM-related health effects.

The authors focused on the collective evidence evaluated in the most recent science review of the PM National Ambient Air Quality Standards and also built upon the evidence presented in previous reviews. The studies examined the health effects primarily due to both short- and long-term exposures to the fine and/or coarse fractions of PM.

Overall, the characteristics of populations most associated with increased susceptibility to PM-related health effects included 1) life stage, specifically children and older adults; 2) preexisting cardiovascular and respiratory diseases; 3) specific genetic polymorphisms; and 4) low socioeconomic status, as measured by educational attainment and income. The authors found more limited evidence suggesting an increase in PM-related health effects in individuals with diabetes, chronic obstructive pulmonary disease, and increased body mass index. Potentially increased risks of PM-related health effects by sex and race/ethnicity also were indicated, although these associations were not consistent across health effects, PM size fractions, or, in some instances, study locations.

The authors concede they are unable to clearly state the overall strength of the evidence for some characteristics of potentially susceptible populations due to inconsistent evidence across epidemiologic studies as well as lack of information from experimental studies regarding biologically plausible mechanisms.

However, the novel integrative approach used to identify characteristics of populations potentially susceptible to PM may be a valuable assessment tool for other air pollutants. The authors also propose a comprehensive definition of “susceptibility” to encompass all populations potentially at increased risk of adverse health effects as a consequence of exposure. Use of such a standardized definition could help reverse inconsistencies in terminology within the epidemiologic literature that may have complicated the identification of high-risk populations to date.

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authors of this study focused on miRNAs because earlier studies linked miRNA disturbances to a number of diseases including blood and solid-tumor cancers. miRNAs act like molecular switches, turning on or off genes, including ones that lead to or protect from disease.

Nearly all the formaldehyde that humans inhale is absorbed in the respiratory tract because the gas is water-soluble and highly reactive. The authors therefore exposed human lung epithelial cells to formaldehyde gas at an air–liquid interface that mimics the human respiratory tract lining.

Of more than 500 miRNAs assessed, formaldehyde significantly downregulated 89 that are predicted to influence molecular signaling pathways relevant to cancer, inflammatory response, and endocrine system regulation, potentially representing a first step on the path toward disease. There is also preliminary evidence that the miRNAs that appeared to be most strongly affected by formaldehyde also may be altered in some cancer cells, suggesting a potential mechanism for the chemical's carcinogenicity.

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